

Appl. No. : 09/832,786
Filed : April 11, 2001

REMARKS

The Applicants have herein cancelled Claims 6-10. New Claims 16 and 17 have been added. The new claims include the limitations of counting the number of ligands in at least one cluster and rating complementarity of the combinatorial library to the target molecule based on the count. Support for these limitations may be found in the specification, for example, in Paragraphs 87 and 88 and Table 7. Claims 1-5 and 11-17 are pending in the application. The Applicants have carefully considered all of the Examiner's rejections but respectfully submit that the claims are allowable for at least the following reasons.

Rejections under § 112 – Indefiniteness

The Examiner rejected Claims 6-10 under 35 U.S.C. § 112, ¶ 2 as being indefinite. The Examiner argued that the "means for" limitations in the claims were not specifically defined in the specification. Although the applicant's disagree with the Examiner's rejection on this point, the Applicants cancel Claims 6-10 with this amendment, thereby rendering the Examiner's rejections moot, without prejudice to continuing prosecution of this subject matter in a continuation application.

Rejections under § 103

The Examiner rejected Claims 1-3, 5-8, 10-13, and 15 under 35 U.S.C. § 103(a) as being obvious over Ho et al. (1994) taken with Rarey et al. (J. Mol. Biol., 1996, hereinafter "Rarey"). The Examiner also rejected Claims 1-15 under 35 U.S.C. § 103(a) as being obvious over Ho taken with Rarey in view of Aldenderfer et al. (1984). The Examiner withdrew the rejections based on Rarey et al. (J. of Computer Aided Molecular Design, 1996). The Examiner argued that Ho describes compound databases having a combinatorial assortment of building blocks and that Rarey discloses that its approach "is fast enough for screening larger sets of ligands for their binding affinity to a given receptor." Rarey, page 472, column 1, lines 21-23. However, although Ho discloses databases of chemical compounds and Rarey discloses screening sets of ligands, neither Ho nor Rarey disclose forming clusters of multiple ligands and rating complementarity of a combinatorial library based on the clusters.

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A *prima facie* case of obviousness requires that all of the claim limitations are taught or suggested by the prior art. See M.P.E.P. § 2143.03. Claim 1 requires forming clusters of ligands from a plurality of ligands and then rating complementarity of a combinatorial library based on the clusters. Similarly, Claim 6 requires means for forming clusters of ligands and means for rating complementarity of a combinatorial library based on the clusters and Claim 11 requires a program storage device embodying a program of instructions that include forming clusters of ligands and then rating complementarity of a combinatorial library based on the clusters. None of these limitations are disclosed by Ho or Rarey.

As recognized by the Examiner, Ho does not disclose determining rms deviation, forming clusters, or rating complementarity of a combinatorial library. Rarey does not provide these missing elements. Instead, Rarey discloses cluster formation only in the context of clusters of different placements of a selected fragment of *a single ligand*. See e.g., Rarey, pages 474-475. Although Rarey implies that the method can be repeated for several ligands in a set of ligands, Rarey does not disclose that results obtained for multiple ligands are clustered with each other. In Rarey, a ligand is docked to a binding site by first docking a selected fragment of that ligand into a binding site. Other fragments of the same ligand are then added to the previously docked fragment until the complete ligand has been assembled in the binding site. The clustering performed by Rarey involves finding a discrete set of distinct orientations for the first fragment from which further ligand building takes place. Forming clusters based on docked positions *of a plurality of ligands* as set forth in Claim 1 is not performed by Rarey.

Accordingly, Rarey indicates that the problem it seeks to solve is "How can a particular ligand be docked into the binding pocket of a given protein?" Rarey, page 470, column 1, lines 14-15. It does this by presenting "a new docking method." Rarey, page 471, column 2, line 20. In contrast, the present invention is not based on a new docking method, but rather directed to assessing combinatorial library complementarity. Rarey does not seek to solve, nor does it disclose how to solve, the problem of assessing combinatorial library complementarity. Rarey does not disclose forming clusters of ligands and then rating library complementarity. Similarly, Ho does not disclose analyzing the docking of multiple ligands and then rating library

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complementarity. Accordingly, one of skill in the art would not be motivated by Ho and Rarey to cluster multiple ligands in order to rate complementarity.

The Applicants respectfully submit that the combination of Rarey and Ho does not disclose all of the limitations of Claims 1-15. Aldenderfer does not disclose the missing limitations. Therefore, the Applicants respectfully submit that Claims 1-15 are not obvious over Ho, Rarey, and Aldenderfer.

New Claims 16 and 17

New independent Claim 16 includes the limitation that the number of ligands in at least one cluster is counted, and the rating is based at least in part on the count. This limitation is also not taught or suggested by the prior art of record. Claim 17 depends from Claim 16. It is respectfully submitted that these claims are also in condition for allowance.

CONCLUSION

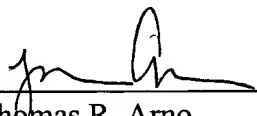
By the foregoing remarks, the Applicants respectfully submit that they have overcome the Examiner's rejections and request a timely issuance of a Notice of Allowance.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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